ABSTRACT

The development of inhibitory antibodies to blood coagulation factor VIII (fVIII) results in a severe bleeding tendency. These antibodies arise in patients with hemophilia A (hereditary fVIII deficiency) who have been transfused with fVIII. They also occur in non-hemophiliacs, which produces the condition acquired hemophilia. We describe a method to construct and express novel recombinant fVIII molecules which escape detection by existing inhibitory antibodies (low antigenicity fVIII) and which decrease the likelihood of developing inhibitory antibodies (low immunogenicity fVIII).

In this method, fVIII is glycosylated at sites that are known to be antibody recognition sequences (epitopes). This produces the desired properties of low antigenicity fVIII and low immunogenicity fVIII. The mechanism is similar to one used by viruses such as the AIDS virus, which glycosylates its surface proteins to escape detection by the immune system.